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MERCHANT & GOULD PC			HILL, KEVIN KAI	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/800,043	OPPERMAN ET AL.
	Examiner	Art Unit
	Kevin K. Hill, Ph.D.	1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 26 March 2007.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-57 is/are pending in the application.
 4a) Of the above claim(s) 3-6,22-41 and 46-57 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1,2,7-21 and 42-45 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

Amendments

Applicants' amendments to Claim 9 in the reply filed March 26, 2007, is acknowledged.

1. Claims 1-2, 7-21 and 42-45 are under consideration.

Specification

2. **The prior objection to the specification is withdrawn** because Applicant has amended the specification to properly denote the trademark TWEEN 20.

Claim Objections

3. **The prior objection to Claim 9 is withdrawn** because Applicant has amended the claim to include the article "a" between the terms "comprising" and "compound".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. **Claims 1-2, 7-9, 16 and 19-20 stand rejected under 35 U.S.C. 102(b)** as being anticipated by Kretz (U.S. Patent No. 6,110,719).

The claims are drawn to a composition comprising a buffer effective for maintaining a pH of aqueous composition at greater than or equal to about 6, and an organic anion of Formula I, wherein the instantly elected embodiment has the structure of Formula III, also known in the art as phytate or hexaphosphate.

With respect to Claims 1-2, 7-8, 16, and 19-20, Kretz teaches a composition comprising sodium phytate in a Tris HCl buffer, pH 7.5 (column 3, lines 32-40).

With respect to Claim 9, Kretz teaches that the composition comprises the phytase enzyme (column 3, line 33), wherein the instant specification discloses that compositions suitable for being immobilized on a support include biomolecules such as proteins (pg 12, lines 10-13 and 23-25).

Thus, Kretz anticipates Claims 1-2, 7-9, 16 and 19-20.

Applicant's Arguments

Applicant argues that the phytate of Kretz et al does not inherently possess the inherent property of being effective to substantially decrease ring formation upon drying of a spot less

Art Unit: 1633

than or equal to about 300 μ m diameter on a support because phytase is also present in the buffer, and would likely hydrolyze phytate to inositol and inorganic phosphate, wherein the hydrolysis is likely to affect the ability of phytate to reduce spot size.

Applicant's argument(s) has been fully considered, but is not persuasive. Applicant's argument is mere allegation without supportive evidence. There is no demonstration that phytate is in fact hydrolyzed by phytase in the buffer of Kretz et al. Even if one were to assume phytase has enzymatic activity, there is no evidence to what degree the phytase is capable of hydrolyzing phytate. Furthermore, the claims do not recite the critical concentration required for phytate to be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 μ m diameter on a support. As such, even if some phytate was hydrolyzed by phytase, there is no evidence that the remaining phytate that is not hydrolyzed would be insufficient to fulfill the instant functional limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. **Claims 1-2 and 7-21 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Kretz et al (Eur. F. Physiol. 439(Suppl): R66-67, 2000) and Veraart et al (J. Chromatography A, 768: 307-313, 1997).

Kretz et al teach nucleic acid hybridization compositions comprising nucleic acids, e.g. DNA, RNA, or mixtures thereof, the compositions further comprising an anionic surfactant SDS, inorganic phosphate and sodium phosphate, pH 7.0, and/or inorganic surfactants extant in Denhardt's Solution (Materials and Methods, pgs 66-67, joining ¶).

Art Unit: 1633

Kreft et al do not teach the composition(s) to comprise phytic acid; however, at the time of the invention, Veraart et al taught the use of phytic acid with a pH buffer comprising inorganic phosphate at pH 7.5 (pg 308, column 2, ¶2.4.1). Veraart et al taught that phytic acid is a large, polyionic molecule whose ionic strength is relatively large as compared with its concentration (pg 307, column 2, lines 7-11).

Veraart et al do not teach that phytic acid will be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 micrometer diameter on a support, as recited in Claim 1. However, it is understood that the recited property is an inherent property of phytic acid, not a structural limitation, and thus the composition of Kreft et al, modified by including phytic acid as taught by Veraart et al, would have the recited effects.

It would have been obvious to one of ordinary skill in the art to modify the hybridization buffer of Kreft et al with the phytic acid of Veraart et al with a reasonable chance of success because the art recognized the growing popularity of phytic acid as a buffering agent (see Abstract, line 1). An artisan would be motivated to include phytic acid in a nucleic acid hybridization composition because phytic acid has a relatively large ionic strength as compared with its concentration (pg 307, column 2, lines 7-11), and the art recognizes that increasing ionic strength can reduce non-specific adsorption to a support (pg 307, column 1). The availability of twelve acidic groups with pKa values ranging from 1.9-9.5 provides the possibility to use phytic acid not only as an additive to suppress wall adsorption effects, but also to control the pH (pg 308, column 1, lines 4-8). Furthermore, the decreased adsorption properties afforded by phytic acid would increase the specific hybridization signal to noise ratio, and thus would be advantageous in hybridization assays.

Thus, the invention as a whole is *prima facie* obvious.

Applicant's Arguments

Applicant argues that:

a) Veraart et al teach the use of phytic acid to prevent an analyte protein from attaching to capillary walls; whereas, the instant invention is concerned with attaching a molecule to a substrate, wherein the substrate comprises reactive groups to immobilize the desired molecule, not preventing such an attachment. There is no teaching or suggestion by Veraart et al that phytic acid can prevent migration of molecules to outer perimeters of spots of print buffer, which proceeds by a mechanism distinct and unrelated to non-specific absorption. There is no connection between prevention of non-specific absorption and improved spot morphology, thus in combining the cited art, there would be not reasonable expectation of successfully producing improved spot morphology.

b) Veraart et al is not analogous art because the use of phytic acid to reduce non-specific hybridization of protein to capillary walls is not pertinent to the problem of spot morphology.

Applicant's argument(s) has been fully considered, but is not persuasive.

With respect to a), the cited prior art teaches all the structural limitations of the claims and the motivation to combine. That the properties of phytate buffers were evaluated via the method of capillary electrophoresis does invalidate the teachings of Veraart et al because the instant invention is a composition, not a method of forming spots. That Veraart et al does not teach the migration mechanism to be solved by phytate is not germane because such functional properties are inherent in phytate. The artisan need not use the composition as contemplated by Applicant. Rather, the artisan may use the composition for protein blotting, for example.

With respect to b), in response to applicant's argument that Veraart et al is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the claims are drawn to a buffer composition comprising phytate. Veraart et al teach the evaluation of phytate as a buffer additive. The instantly claimed composition further comprises a compound suitable for being immobilized on a support. The proteins carried by the phytate buffer of Veraart et al are suitable for being immobilized on a support. Thus, it is the Examiner's position that Veraart et al is *bona fide* analogous art for teaching a buffer composition comprising phytate and compounds, specifically proteins, suitable for being immobilized on a support.

6. **Claims 1 and 14-15 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Kretz (U.S. Patent No. 6,110,719) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989).

The claims are drawn to a composition comprising a buffer effective for maintaining a pH of aqueous composition at greater than or equal to about 6, and an organic anion of Formula I, wherein the instantly elected embodiment has the structure of Formula III, also known in the art as phytate or hexaphosphate, wherein the buffer further comprises inorganic phosphate.

Kretz teaches a composition comprising sodium phytate in a Tris HCl buffer, pH 7.5 (column 3, lines 32-40). Kretz does not teach the composition to comprise inorganic phosphate; however, at the time of the invention, Sambrook et al taught how an artisan may create phosphate buffered solutions using sodium phosphate and/or potassium phosphate (pg B.21, Tables B.10 and B.11; see also pg B.12 for recipe).

Art Unit: 1633

It would have been obvious to one of ordinary skill in the art to modify the buffer of Kretz with the inorganic phosphate-providing buffer of Sambrook et al with a reasonable chance of success because Sambrook et al teach how to make a phosphate buffer with a buffering capacity at pH 7.5. An artisan would be motivated to substitute the Tris-HCl buffer of Kretz with the phosphate buffer of Sambrook et al because the phosphate buffer would provide a greater amount of inorganic phosphate groups into the composition and enhance the activity and buffering capacity of the phytic acid.

Thus, the invention as a whole is *prima facie* obvious.

Applicant's Arguments

Applicant argues that:

- a) Kretz does not suggest the use of phytate as a buffering agent or buffer additive,
- b) the Examiner did not address the limitation of the claim to the organic anion's ability to substantially decrease ring formation upon drying of a spot less than or equal to about 300 μ m in diameter,
- c) Kretz is non-analogous art, related to enzymes and nutrition, that is quite distinct and unrelated to the field of the present invention.

Applicant's argument(s) has been fully considered, but is not persuasive.

With respect to a), the claims are drawn to a composition comprising a buffer, phytate and inorganic phosphate. The cited prior art teach such structural limitations, and a motivation to combine the references has been provided. It is not necessary that the artisan use the composition as contemplated by Applicant, as the claims are not method claims.

With respect to b), the Examiner regrets the inadvertent error of failing to iterate the inherent property possessed by phytate as established and set forth earlier in the office action to fulfill the functional limitations. The Examiner's response to Applicant's traverse of the inherency argument discussed above is iterated presently. "Applicant's argument is mere allegation without supportive evidence. There is no demonstration that phytate is in fact hydrolyzed by phytase in the buffer of Kretz et al. Even if one were to assume phytase has enzymatic activity, there is no evidence to what degree the phytase is capable of hydrolyzing phytate. Furthermore, the claims do not recite the critical concentration required for phytate to be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 μ m diameter on a support. As such, even if some phytate was hydrolyzed by phytase,

Art Unit: 1633

there is no evidence that the remaining phytate that is not hydrolyzed would be insufficient to fulfill the instant functional limitations.”

With respect to c) in response to applicant's argument that Kretz is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the claims are drawn to a buffer composition comprising phytate. Kretz teaches a buffer comprising phytate. Thus, it is the Examiner's position that Kretz is *bona fide* analogous art for teaching a buffer composition comprising phytate. The allegation that Kretz would not have commended the attention of some artisans in the field of drug delivery coatings or array technology is not germane, because the intended use of the phytate buffer composition holds no patentable weight.

7. **Claims 42-45 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Diehl et al (Nucleic Acids Research 30(16): e79, pgs 1-6, 2002) and Veraart et al (J. Chromatography A, 768: 307-313, 1997).

Diehl et al teach a method of forming spots of a composition on a surface, the method comprising a nucleic acid and a buffer effective for maintaining pH of aqueous composition equal to or about pH 7.5 (pg 2, column 1, ¶3). Diehl et al teach the method of spotting to comprise pin spotting machines (pg 2, column 1, ¶4).

Diehl et al do not teach the buffer to comprise phytic acid; however, at the time of the invention, Veraart et al taught the use of phytic acid with a pH buffer comprising inorganic phosphate at pH 7.5 (pg 308, column 2, ¶2.4.1). Veraart et al taught that phytic acid is a large, polyionic molecule whose ionic strength is relatively large as compared with its concentration (pg 307, column 2, lines 7-11).

Neither Diehl et al or Veraart et al teach that the buffer, specifically comprising phytic acid, will be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 micrometer diameter on a support, as recited in Claim 42. However, it is understood that the recited property is an inherent property of phytic acid, not a structural limitation, and thus the method and buffer of Diehl et al, modified by including phytic acid as taught by Veraart et al, would have the recited effect.

An artisan would be motivated to include phytic acid in a method of spotting organic compositions such as nucleic acids because phytic acid has a relatively large ionic strength as compared with its concentration (pg 307, column 2, lines 7-11), and the art recognizes that increasing ionic strength can reduce non-specific adsorption to a support (pg 307, column 1). The availability of twelve acidic groups with pKa values ranging from 1.9-9.5 provides the possibility to use phytic acid not only as an additive to suppress wall adsorption effects, but also

Art Unit: 1633

to control the pH (pg 308, column 1, lines 4-8). Furthermore, large, polyionic molecules are preferable because they provide high ionic strengths at relatively low currents (pg 307, joining ¶¶). With relatively small ions used to enhance the ionic strength, the associated increment of the electric current is rather dramatic, resulting in the Joule heating effect. The Joule heating effect extant in piezoelectric delivery devices would be minimized in the presence of phytic acid, thus minimizing or avoiding unwanted heating of the composition that is to be deposited onto the support.

Thus, the invention as a whole is *prima facie* obvious.

Applicant's Arguments

Applicant argues that:

- a) Diehl et al do not cure the deficiencies of Veraart et al, and
- b) an artisan reading Veraart et al would not conclude that there might be a benefit derived from the addition of phytic acid to an array spotting buffer.

Applicant's argument(s) has been fully considered, but is not persuasive.

With respect to a), In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that Diehl et al does not teach or suggest the use of phytate to produce arrays with reduced spot size, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). The intended use of phytate in a spotting buffer for reasons other than those contemplated by Applicant would yield substantially decreased ring formation upon drying of the spot given the inherent properties of phytate discussed above.

With respect to b), the opinion is unsubstantiated, and there is no evidence that such a conclusion held by Applicant would speak for all artisans in the field.

Art Unit: 1633

8. **Claims 42 and 45 are rejected under 35 U.S.C. 103(a)** as being unpatentable over the prior cited art as applied to Claim 42 above, and in further view of Lemieux et al (* of record in IDS).

The prior cited art does not teach the method of forming spots, wherein the applying step comprises pin piezoelectric spotting.

However, at the time of the invention, Lemieux et al summarized DNA chip-making technologies, stating that one may produce microarrays by mechanical microspotting by pins (pg 281, column 2, ¶1) or by ink-jet nozzles that rely on the piezoelectric effect (pg 281, column 2, ¶4).

It would have been obvious to one of ordinary skill in the art to substitute pin spotting methods, as taught by Diehl et al, with spotting methods using the piezoelectric effect, as taught by Lemieux et al with a reasonable chance of success because the art recognized that such technology was available at the time. An artisan would be motivated to use piezoelectric spotting equipment, e.g. ink-jet, because the electric current can be precisely controlled, and thus the artisan can precisely control the amount of fluid that is taken up by the quill and dispensed onto the support, obtaining exceptional control of both quality and reproducibility.

Thus, the invention as a whole is *prima facie* obvious.

Applicant's Arguments

Applicant argues that although Lemieux et al teach pin piezoelectric spotting, Lemieux et al does not cure the deficiencies of Diehl et al and Veraart et al previously discussed.

Applicant's argument(s) has been fully considered, but is not persuasive.

Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that Diehl et al does not teach or suggest the use of phytate to produce arrays with reduced spot size, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). The intended use of phytate in a spotting buffer for reasons other than those contemplated by Applicant would yield substantially

decreased ring formation upon drying of the spot given the inherent properties of phytate discussed above.

Conclusions

9. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kevi Fawcett

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